

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

14
REC'D 01 OCT 2001

WIPO

PCT

| | | |
|--|--|---|
| Applicant's or agent's file reference RTSP-0034 | FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/116) | |
| International application No. PCT/US99/29569 | International filing date (day/month/year) 14 DECEMBER 1999 | Priority date (day/month/year) 21 JULY 1999 |
| International Patent Classification (IPC) or national classification and IPC Please See Supplemental Sheet. | | |
| Applicant ISIS PHARMECEUTICALS, INC. | | |

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

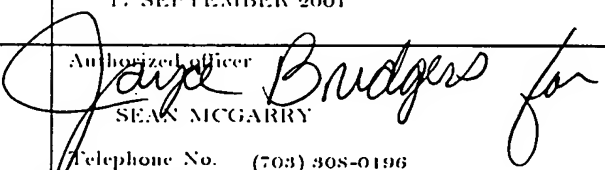
2. This REPORT consists of a total of 4 sheets.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of _____ sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of report with regard to novelty, inventive step or industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

| | |
|--|---|
| Date of submission of the demand 15 FEBRUARY 2001 | Date of completion of this report 17 SEPTEMBER 2001 |
| Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 | Authorized officer  SEAN MCGARRY |
| Facsimile No. (703) 305-3230 | Telephone No. (703) 308-0196 |

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US99/29589

I. Basis of the report**1. With regard to the elements of the international application:***☒ the international application as originally filed☒ the description:pages 1-81, as originally filedpages NONE, filed with the demandpages NONE, filed with the letter of _____☒ the claims:pages 82-83, as originally filedpages NONE, as amended (together with any statement) under Article 19pages NONE, filed with the demandpages NONE, filed with the letter of _____☒ the drawings:pages NONE, as originally filedpages NONE, filed with the demandpages NONE, filed with the letter of _____☒ the sequence listing part of the description:pages 1-12, as originally filedpages NONE, filed with the demandpages NONE, filed with the letter of _____**2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.**

These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).☐ the language of publication of the international application (under Rule 48.3(b)).☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).**3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:**☒ contained in the international application in printed form.☒ filed together with the international application in computer readable form.☐ furnished subsequently to this Authority in written form.☐ furnished subsequently to this Authority in computer readable form.☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.**4. ☒ The amendments have resulted in the cancellation of:**☒ the description, pages NONE☒ the claims, Nos. NONE☒ the drawings, sheets 44 NONE**5. ☐ This report has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).****

* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

**Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US99/29589

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability, citations and explanations supporting such statement**1. statement**

| | | | |
|-------------------------------|--------|-----------------------|-----|
| Novelty (N) | Claims | <u>1-16</u> | YES |
| | Claims | <u>NONE</u> | NO |
| Inventive Step (IS) | Claims | <u>3, 4, and 16</u> | YES |
| | Claims | <u>1, 2, and 5-15</u> | NO |
| Industrial Applicability (IA) | Claims | <u>1-16</u> | YES |
| | Claims | <u>none</u> | NO |

2. citations and explanations (Rule 70.7)

Claims 1, 2, and 5-15 lack an inventive step under PCT Article 33(3) as being obvious over Davis et al (US 5,736,381). Davis et al disclose a nucleic acid sequence encoding MKK which is the equivalent of the Jun N-terminal kinase kinase of the instant invention. Davis et al disclose in column 3, for example that MKK can be targeted by antisense oligonucleotides and that these antisense oligonucleotides can be about 15 nucleotides in length. The modification of antisense oligonucleotide sugars bases and backbones was well known and routinely done in the art at the time the instant invention was made.

Claims 3, 4 and 16 meet the criteria set out in PCT Article 33(2)-(4), because the prior art does not teach or fairly suggest the specific antisense sequences of claims 3 or 4 and does not provide sufficient guidance for a method of treating disease with antisense targeted to Jun N-terminal kinase kinase.

----- NEW CITATIONS -----
none

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US99/29589

Supplemental B x

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

Sheet 10

CLASSIFICATION:

The International Patent Classification (IPC) and/or the National classification are as listed below:

IPC(7): C07H 21/04; C12N 15/00; C12Q 1/68 and US Cl.: 435/6, 91.1, 91.31; 536/23.1, 24.1, 24.5